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10/030,202	12/27/2001	Frans Eduard Janssens	JANS-0027	9001

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EXAMINER	
HABTE, KAHSAY	

ART UNIT	PAPER NUMBER
1624	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/030,202	Applicant(s) JANSSENS ET AL.	
	Examiner Kahsay Habte, Ph. D.	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6,8-15 and 18-22* is/are pending in the application.

4a) Of the above claim(s) 22 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,8-15 and 18-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-4, 6, 8-15 and 18-22 are pending.

Response to Amendment

2. Applicant's amendment filed 9/4/03 in response to the previous Office Action (Paper No. 11) is acknowledged. Rejections of claims 1-4, 6, 8-15 and 8-21 under 35 U.S.C. § 112, second paragraph (Paper No. 11, paragraphs 6a-6e) have been obviated.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 11-12 are rejected under 35 U.S.C. 102(b) as being anticipated by Janssens et al. (US Pat No. 5,360,807). The instantly claimed method of manufacturing medicament comprising compounds of formula (I) reads on the composition of the reference. See the compounds disclosed in TABLE 2-4 (columns 25-34). The reference teaches the pharmaceutical compositions, see the disclosure on column 19 (lines 6-18). The reference clearly teaches that the compounds were prepared to be used in pharmaceutical field (as an active antiallergic e.g. asthma and antihistaminic).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2-4, 10-11, 13 and 15-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Janssens et al. (US Pat No. 5,360,807). The reference discloses compounds such as 1-[(6-methyl-2-pyridinyl)methyl]-2-(4-piperdinyloxy)-1H-Benzimidazole; 1-[(6-methyl-2-pyridinyl)methyl]-2-(4-piperdinylmethyl)-1H-Benzimidazole, which have been excluded from the instant claims, see the last line of claim 2. The instant claims, however, include compounds that are homologues of the reference compounds, i.e., compounds that differ by a -CH_2 group (i.e., adding or removing a methyl substituent to or from the reference compounds, e.g., adding a –CH2- group to the pyridyl substituent to the species 1-[(6-methyl-2-pyridinyl)methyl]-2-(4-piperdinyloxy)-1H-Benzimidazole. The reference teaches that the compound is useful as an active antiallergic and antihistaminic agent for the treatment of warm-blooded animals suffering from allergic diseases. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous compounds would be expected to possess similar utilities. It has been held that compounds that are structurally homologous to prior art compounds are prima facie obvious, absent a showing of unexpected results. *In re Haas*, 60 USPQ

544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950). *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990).

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 10 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. There has been recited a method of treating viral infections, but the specification is not enabled for such a scope.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The scope of the claims is not adequately enabled solely based on the activity related to antiviral activity provided in the specification. First, the instant claims cover

'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The use disclosed in the specification is as pharmaceutical therapeutic agents having antiviral activity, useful to treat viral infections in general. Test procedures and assays are provided in the specification at page 91 only for 11 compounds and it is concluded that the representative compounds of formula (I) demonstrated positive inhibitory activity with IC_{50} ranging from 0.00013 μM to 2.51119 5 μM, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of the diverse disorders embraced the instant claims. The disorders encompassed by the instant claims (i.e. viral infections in general), some of which have been proven to be extremely difficult to treat. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

The claims are drawn to 'treating **viral infections** ', however, there is no common mechanism by which all conditions due to viral infections arise. There are more than 400 distinct viruses that infect humans producing a wide range of diseases. Cecil Textbook of Medicine states that "for many viral infections, no specific therapy exists. Proper use of antivirals requires specific viral diagnosis" (see the enclosed article, page 1742).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4, 6, 8-11 and 12-15 and 18-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention:

a. Claim 1 and claims dependent thereon are rejected because the phrase "a method of manufacturing a medicament for the treatment of viral infections, comprising the step of providing.." is not clear. The claim starts as a method claim, but it ends up as a composition claim. If it is a method claim then it should be written in method claim language by reciting all the steps of manufacturing medicaments. Note that the term "providing" does not replace the steps required for the manufacture of the medicament..

b. Claim 2 and claims dependent thereon are rejected because the term "prodrug" is indefinite. Determining whether a given derivative definitely is or is not a prodrug involves more than routine experimentation. If the derivative is active, open-ended experimentation may be involved to determine for sure whether the compound is a prodrug or whether it is active in its own right.

c. Claims 10-11 and 13 are rejected because they depend on cancelled claims. Note that claims 5 and 7 are cancelled claims.

Claim Objections

7. Claim 12 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from other multiple dependent. For example, claim 12 cannot multiply dependent on claim 10 that is multiply dependent. See MPEP § 608.01(n).

Conclusion

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte, Ph. D. whose telephone number is (703) 308-4717. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Kahsay Habte, Ph. D.
Examiner
Art Unit 1624

DEEPAK RAO
PRIMARY EXAMINER

Mukund J. Shah
Supervisory Patent Examiner
Art Unit 1624

KH
October 6, 2003